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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/646,835	01/11/2001	Gabriele Multhoff	40740	1173

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EXAMINER
CANELLA, KAREN A

ART UNIT	PAPER NUMBER
1642	16

DATE MAILED: 12/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/646,835	Multhoff
Examiner	**Art Unit**
Karen Canella	1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3 months* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☐ Responsive to communication(s) filed on _____.

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *31-60* is/are pending in the application.

4a) Of the above, claim(s) *43 and 49* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *31-42, 44-48, and 50-60* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 1
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Acknowledgment is made of applicants election with traverse of species a, drawn to cancerous diseases. The traversal is on the grounds that all the claimed species, cancerous diseases, autoimmune diseases and infectious diseases, share Unity of Invention as they are all linked by the special technical feature of activation of NF cells by Hsp70 protein or fragments and derivatives thereof, and that review of all independent claims demonstrates that said activation /modulations links the invention as a whole. This has been considered but not found persuasive. Claims 50-53 are drawn to pharmaceutical compositions comprising the Hsp70 protein and do not embody the limitation of activating NK cells. Furthermore, as demonstrated by the art rejections below, the claimed methods and compositions lack novelty over the art and thus claims drawn to methods of treatment comprising administering the Hsp70 protein, cells expressing said protein and compositions of Hsp70 protein do not share a special technical feature.

2. For these reasons the species election requirement is deemed to be proper and is adhered to. The requirement is therefore made FINAL.

3. Claims 1-30 have been canceled. Claims 31-60 have been added. Claims 43 and 49, drawn to non-elected species, are withdrawn from consideration. Claims 1-42, 44-48 and 50-60 are examined on the merits.

Claim Objections

4. Claims 37, 43, 48 and 53 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 42 reciting the specific embodiments of administering the NK cell obtained by the method of claim 37. Claim 43 embodies a patient suffering from a cancerous disease. Claim 48 embodies the method of claim 43, wherein the cancerous diseases are tumors, solid tumors, metastatic tumors, leukemias and lymphomas. However, claim 37 is dependent upon claim 36 which specifically embodies leukemia cells, lymphoma cells, tumor cells, metastasizing cells of solid tumors. Claim 36 is dependent upon claim 35 which specifically embodies cancerous cells from a patient (due to the election requirement of "a cancerous disease"). Thus claims 43 and 48 do not further limit claim 42 as the specific embodiments of claims 43 and 48 are already present in claim 43.

Claim 37 contains a typographical error "the method of any one of claims 36". For purpose of examination, the claim will be read as --the method of claim 36---.

Claim Rejections - 35 USC § 112

5.The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 30-42, 44-48 and 50-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 53 recites "the method of claim 50, wherein said protein or fragment is recombinant". It is unclear how the origin of the protein, natural, synthetic or recombinant, serves to modify the characteristics of the claimed composition.

Claims 31, 42, 50 and 55 recite "derivatives" of Hsp70 or the fragment of Hsp70 from amino acid 384-641, or amino acid sequences having 70% homology to the aforesaid fragment. The specification neither defines or provides examples of a "derivative", therefore, the metes and bounds of the claims with respect to the constitution of a derivative cannot be ascertained.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 30-42, 44-48 and 50-60 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

(A)As drawn to new matter.

Newly submitted claims 44 and 57 specifically embody the administration to a patient of an Hsp70 protein and/or NK cells activated by an Hsp70 protein, wherein the administration is carried out for at least three hours. Originally submitted claim 13 is cited as providing support fro these new claims. However, original claim 13 is drawn to the ex vivo incubation of a suspension of natural killer cells and Hsp70 protein for at least 3 hours and provides no enablement for a method wherein the administration of NK cells activated by Hsp70, or the administration of Hsp70 protein is carried out over the course of at least three hours. Further, the specification describes and i.p. or o.t. injection of the activated killer cells into SCID mice, but does not teach that the injection should be carried out over the course of three hours. One of skill of the art would reasonably conclude that applicant was not in procession of the specific embodiments of claims 44 and 57 at the time the invention was filed.

(B)As drawn to derivatives of the amino residues 284-641 of SEQ ID NO:1, proteins having 70% homology to amino acids 384-641 of SEQ ID NO:1, and derivatives thereof.

Claims 31-42, 44-48 and 50-60 are drawn to a genus of proteins comprising derivatives of proteins having the amino acid sequence from residues 384-681 of SEQ ID NO:1 and proteins having at least 70% homology to amino acid residues 384-641 of SEQ ID NO:1 and derivatives thereof, as well as method claims dependent upon these products. The specification sets forth

Hsp70 as SEQ ID NO:1, and teaches that residues 384-641 of SEQ ID NO:1 are responsible for the activation of NK cells into cytotoxic cells. The specification teaches that the Hsp70 protein is a heat shock protein which is differentially expressed on many types of cancerous cells. The specification contemplates methods of activating NK cells by means of proteins having at least 70% homology to amino acid residues 384-681 of SEQ ID NO:1. The specification also contemplates "derivatives" of Hsp70 or the fragment of Hsp70 from amino acid 384-641, or amino acid sequences having 70% homology to the aforesaid fragment. The specification states on page that the term "derivative" encompasses both derivatives of the Hsp70 protein as well as derivatives of the C-terminal fragment as far as the derivatives exhibit the function of the invention. However, the specific limitation with regard to said function is missing from the claims, and further, the specification provides no teachings regarding the structural attributes of what constitutes a "derivative" of the claimed proteins which would serve to discriminate between members of the claimed genus and species which were not part of the claimed genus. The genus is therefore highly variant encompassing widely ranging structural deviations from Hsp70 and the amino acid sequence comprising residues 284-681 of SEQ ID NO:1, wherein said deviations could include fusions with any other amino acid sequence, alterations of the protein backbone, coupling with any known chemical which reacts with amino acid sequences, proteolytic fragments of the amino acid sequence comprising residues 284-641 of SEQ ID NO:1, enzymatic modification of said amino acid sequence, and amino acid substitutions, deletions and additions to residues 281-641 of SEQ ID NO:1. The disclosure of SEQ ID NO:1 is inadequate written description for this multitude of species encompassed by the claims..

The specification states on page 4, that amino acid sequence identity to the Hsp70 protein means that at least 70% of the amino acids are identical when the two amino acid are aligned, wherein one of the aligned sequences is the C-terminus of Hsp70. The specification also states that the invention encompasses sequences which have 70% identical amino acids, but differ by gaps when aligned with the Hsp70 sequence, and that said gaps can occur in the homologous

molecule or in the reference molecule. Thus, the specification teaches that 70% homologous sequences encompasses amino acid sequences which have substitutions, deletions and additions of amino acids from amino acid residues 384-681 of SEQ ID NO:1. No further description of any variant protein structure is made by the specification and no embodiment limiting the number of amino acid substitutions, deletions or additions is present in the specification or claims. Thus the scope of the genus includes numerous structural variants and the genus is highly variant because s significant number of structural differences between genus members is permitted. Neither the specification or claims indicate distinguishing structural and functional characteristics shared by members of the genus that could serve to distinguish proteins in the genus from other proteins not in the genus.

The general knowledge and skill in the art do not supplement the omitted description of derivatives and proteins comprising variants of residues 384-681 of SEQ ID NO:1, and derivatives thereof, because specific, not general, guidance is what is needed. Since the disclosure fails to identify the structural and functional attributes of the genuses, and because the genuses are highly variant, SEQ ID NO:1 alone is insufficient to describe the claimed genus. Furthermore, one of skill in the art would conclude that the specification also failed to describe a number of species representative of the "derivative" genus and the "70% homologous" genus. Thus, applicant was not in possession of the either the claimed "derivative" or "homolog" genuses.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in

section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

10. Claims 50-53 and 55, 56 and 58-60 are rejected under 35 U.S.C. 102(b) as being anticipated by Srivastava (WO 97/10001).

Claim 50 is drawn in part to a pharmaceutical composition comprising the Hsp70 protein or a pharmaceutical composition comprising the amino acids of 384-681 of SEQ ID NO:1, and a pharmaceutically acceptable carrier, excipient or diluent. Claim 51 embodies the composition of claim 50, wherein said protein or fragment is present at a concentration of about 10 micrograms/ml to 1000 micrograms per ml. Claim 52 embodies the composition of claim 50 wherein said protein or fragment is of human origin. Claim 53 specifically embodies the composition of claim 50, wherein said protein or fragment is recombinant, however, for the reasons set froth in the rejection under 35 U.S.C. 112, second paragraph above, it is unclear how the limitation of "recombinant"can change the specific embodiments of the claim.

Claim 55 is drawn to a method of in vivo activation of the immune system in a patient in need thereof comprising administering to said patient a pharmaceutically effective amount of an Hsp70 protein or a C-terminal fragment of Hsp70 comprising amino acid residues 284-681 of SEQ ID NO:1. Claim 56 embodies the method of claim 55 wherein said patient is suffering from cancer. Claim 58 embodies the method of claim 56, wherein said administration further comprises addition of a cytokine, claim 59 specifies that the cytokine in an interleukin. Claims 60 embodies the interleukins of Il-2, Il-12 and Il-15.

Srivastava discloses a method for eliciting an immune response in an individual in whom the treatment if cancer is desired by administering a composition comprising a heat shock protein, wherein the heat shock protein is human Hsp70 (page 14, line 33 to page 15, line 2 and lines 29-31, page 43, line 15 to page 44, line 12). Srivastava discloses that said method further comprises

the administration of biological response modifiers such as interferons alpha and gamma, interleukins 2, 4, and 6, tumor necrosis factor or other cytokine growth factors in combination with the heat shock protein (page 12, lines 18-22). Srivastava does not specifically state that Hsp70 activates NK cells, however the administration of Hsp70 to a mammal in an amount sufficient to elicit an immune response for the treatment of cancer would inherently activate NK cells in said individual.

Srivastava discloses pharmaceutical compositions comprising Hsp70 in physiologically acceptable solvents for the administration to mammals (page 38, lines 32-35 and page 39, line 30 to page 42, line 15). Srivastava further discloses a composition comprising five to ten micrograms of the Hsp70 protein in 100 microliter, which is the same as 50 micrograms/ml to 100 micrograms/ml and thus falls within the claimed range of 10 micrograms/ml to 1000 micrograms/ml (page 36, lines 25-32).

11. Claims 31-36 are rejected under 35 U.S.C. 102(b) as being anticipated by Multhoff et al (Journal of Immunology, 1997, Vol. 158, pp. 4341-4350) as evidenced by Botzler et al (Cell Stress and chaperones, 1998, Vol. 3, pp. 6-11).

Claim 31 is drawn in part to a method for the ex vivo activation of NK cells comprising contacting NK cells in a physiological suspension with a protein comprising a derivative of the fragment consisting of amino acid residues 284 to 361 of SEQ ID NO:1. Claim 32 embodies the method of claim 31 wherein said activation comprises an increase in cytotoxicity. Claim 33 embodies the method of claim 33 wherein said physiological suspension containing NK cells comprises a peripheral mononuclear blood cell fraction. Claim 34 comprises the method of claim 31 wherein said suspension further comprises cells expressing cell-surface Hsp70. Claim 35 embodies the method of claim 34 wherein said expressing cells comprise diseased cells from a patient. Claim 36 specifies that the diseased cells are selected from tumor cells.

Multhoff et al discloses a method for the ex vivo activation of NK cells comprising contacting an Il-2 stimulated NK cells obtained from fractionation of peripheral blood with colon carcinoma cells. The colon carcinoma cells are a cell line named CX derived from a patient and thus satisfy the specific embodiment of claims 35 and 36. Botzler et al disclose that the CX cell line expresses the Hsp70 antigens and that the C-terminus of Hsp70 is localized extracellularly. Thus the specific embodiment of claim 34 is fulfilled. Multhoff et la disclose that Hsp72 cell surface expression of the CX2 and CX+ colon carcinoma cells strictly correlates with lysis by NK cells (page 4344, under the heading "Cytotoxicity assay", figure 7, page 4349, first full paragraph, and third full paragraph, "on NK cells, one must consider HSP72 expression as an additional possible structure that determines the susceptibility of tumor target cells to lysis is mediated by an NK population"). The specific lysis indicated in figure 2 is indicative of an increase in cytotoxicity, thus fulfilling the specific embodiment of claim 32.

12. Claims 31-37 and 39-41 are rejected under 35 U.S.C. 102(b) as being anticipated by Multhoff et al (Blood, 1995, Vol. 86, pp. 1374-1382). The specific embodiments of claims 31-36 are set forth above. Claim 37 embodies the method of claim 36, wherein the contacting is carried out for at least 3 hours. Claim 39 is drawn to the method of claim 37, wherein the conditions further comprise addition of a cytokine. Claim 40 specifies that the cytokine is an interleukin. Claim 41 specifically embodies the interleukins of Il-2, Il-12 and Il-15.

Multhoff et al discloses a method for the ex vivo activation of NK cells comprising contacting an Il-2 stimulated NK cells obtained from fractionation of peripheral blood (page 1375, second column, under the heading "Separation of effector cell populations") with human sarcoma cells (page 1375, first column, under the heading "Cell culture of normal and malignant cells"). The sarcoma cell line used by Multhoff are derived from derived from patients suffering from cancer and thus satisfy the specific embodiment of claims 35 and 36. Multhoff et al disclose that the sarcoma cells express Hsp72, which is a heat-inducible form of Hsp70 and that the Hsp72 is a

cell surface determinant for NK cells (page 1380, first column, line 20 to second column, line 4). Thus the specific embodiment of claim 34 is fulfilled. Multhoff et la disclose that Hsp72 cell surface expression on the sarcoma cells correlates with lysis by NK cells (figures 1 and 2). The specific lysis indicated in figures 1 and 2 is indicative of an increase in cytotoxicity, thus fulfilling the specific embodiment of claim 32. Multhoff et al disclose the incubation of Il-2 activated NK cells with target cells , wherein the contacting is carried out for 4 hours, fulfilling the specific embodiment of claims 37 and 40-41 (page 1376, first column, under the heading "Cytotoxicity assay").

13. Claims 31-37, 39-41, 50-56 and 58-60 are rejected under 35 U.S.C. 102(e) as being anticipated by Multhoff et al (U.S. 6,261,839). The embodiments of claims 31-37, 39-41, 50-53, 55, 56 and 58-60 are set forth above. Claim 54 is drawn to a pharmaceutical composition comprising NK cells activated by the method of claim 31. Multhoff et al disclose the method of ex vivo activation comprising contacting fractionated NK cells obtained from peripheral blood with target cells selected from the group consisting of leukemic cells, metastasized solid tumor cells and metastasized lymphoma cells (claims 1-18), wherein said target cells are induced to over express the Hsp70 protein. Multhoff et al disclose that enhanced activation of Hsp70 specific NK cells can be achieved by addition of interleukin-2 in a low dose (column 7, lines 65-67). Multhoff et al also disclose a method of treating a subject having cancer comprising administering the NK cells activated by incubation with the target cells expressing the Hsp70 protein (claims 19 and 20). Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 31-37 and 39-42, 43, 48, 50-53, 54-56 and 58-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Multhoff et al (Blood, 1995, Vol. 86, pp. 1374-1382) in view of what is suggested in the Multhoff et al and Srivastava (WO 97/10001).. The embodiments of claims 31-37, 39-41, 50-53, 55, 56 and 58-60 are set forth above. Claim 42 is drawn to a method for the in vivo activation of the immune system of a patient in need comprising administering to said patient a pharmaceutically effective amount of NK cells obtained by the method of claim 37 and optionally administering to said patient a pharmaceutically effective mount of Hsp70 protein. Claim 43 embodies the method of claim 42 wherein said patient is suffering from a cancerous disease. Claim 48 embodies the method of claim 43 wherein said cancerous disease is tumors, solid tumors, metastatic tumors, leukemias and lymphomas.

Multhoff et al teach the specific embodiments of claims 31-37 and 39-41 for the reasons set forth in section 12 above. Multhoff et al do not teach a method for the in vivo activation of the immune system in a pateint in need thereof comprising the administration of NK cells activated by the method of claim 37 or a pharmaceutical composition comprising NK cells activated by the method of claim 31. Multhoff et al do not teach the concurrent or subsequent administration of a Hsp70 protein in addition to the activated NK cells of claim 37. Multhoff et al suggests that NK cells are relevant for recognition of tumor cells expressing heat shock proteins

as published observations indicate that tumors can be infiltrated and killed by NK cells and that metastatic inhibition has been correlated with NK cells (page 1380, second column, lines 10-15).

Srivastava (WO 97/10001) teaches the specific embodiments of claims 50-53 and 55, 56 and 58-60 for the reasons set forth in section 10 above. Srivastava teach the in vivo activation of the immune system in a patient in need of comprising administration of the Hsp70 protein useful for the treatment of leukemia, lymphoma, solid tumors and metastatic tumors (page 43, line 16 to page 44, line 5 and lines 16 to page 46, line 7).

It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to administer the NK cells as a pharmaceutical composition to a patient having a tumor expressing the Hsp72 protein. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Multhoff et al on the cytotoxicity of NK cells to effect lysis to tumor cells expressing surface Hsp72 protein and the suggestion of Multhoff et al that NK cells can infiltrate and kill tumor cells in vivo.

Further It would have been *prima facia* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine the administration of a pharmaceutical composition comprising NK cells with the method of inducing an immune response comprising the administration of the Hsp70 protein. The instant situation is amenable to the type of analysis set forth in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to produce a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been taught individually in the prior art. Applying the same logic to the instant process claims, it would be obvious to one of skill in the art to combine two methods to induce an immune response in order to treat an individual with cancer. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Srivastava on the therapeutic efficacy of treating cancer by the administration of the Hsp70 protein.

Double Patenting

16. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentable distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g. *In re Berg*, 140 F. 3d 1428, 46 USPQ2d 1226 (Fed Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

18. Claims 31-36 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-20 of U.S. Patent No. 6,261,839. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-18 of the '839 patent anticipate the instant claims 31-36. Claims 19 and 20 of the '839 patent

anticipate claims 55 and 56 as the method of administering NK cells of the patent would inherently comprise a pharmaceutically effective amount of a Hsp70 protein.

Conclusion

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Karen A. Canella, Ph.D.
Patent Examiner, Group 1642
December 16, 2002